Remarks

Claims 27-42 and 49-61 are now pending. Non-elected claims 1-26 and 43-48 have been canceled. New claims 49-61 have been added. No new matter has been introduced.

Claims 27-33 and 35-37 have been rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,837,313 to Ding et al. ("Ding"). The Examiner has opined that Ding's mere disclosure of curing the coating followed by subjecting the coating to argon gas plasma and exposure to gamma radiation, electron beam, ethylene oxide or steam sterilization is sufficient to support an obviousness rejection. The Examiner reasoned that (1) absent a showing of criticality of the claimed current density, obviousness "is seen in adjusting the flow rate and power of the argon plasma treatment or electron beam in order to reach the claimed current density"; (2) placing a substrate in a plasma chamber at varying power ranges and flow rates correlates to "directing a beam of charged particles" as claimed; and (3) Ding disclosure would inherently result in an increase in drug release rate from the coating. Applicant believes that this is an accurate summarization of the Examiner's position, as best understood by the Applicant. If the Applicant has mischaracterized the Examiner's position, Applicant respectfully requests for the Examiner to clarify his position, considering that the Applicant will appeal any further rejection of the claims. Applicant would like to be clear about the Examiner's position so that counter arguments can be clearly set forth in the appeal brief.

Before addressing the merits of the rejection, the Examiner noted that "[w]ith respect to the claimed current density, the 'about' modifier has not been defined in the specification. As such, ... 'about 0.001 $\mu A/cm^2$ to about 1 $\mu A/cm^2$ ...' reasonably reads

on any current density being applied." The Applicant respectfully disagrees with the Examiner's position as "about" modifiers are well accepted modifiers and have not been deemed indefinite or vague. However, to push this case towards allowance or for preparing the application for appeal, Applicant has deleted the "about" modifier.

Now, with respect to the substance of the rejection, Applicant respectfully traverses. As indicated in the previous response, claim 27 defines a method of directing a beam of charged particles to the dry polymeric coating to modify the release rate of the active agent from the coating. **The beam of charged particles has a current density from about 0.001 $\mu A/cm^2$ to about 1 $\mu A/cm^2$. The act of directing a beam of charged particles to the dry polymeric coating causes the coating to have an increased release rate of the active agent from the coating**. As described in the specification, the beam of charged particles in the recited range of current density allows the claimed method to **increase the release rate of the active agent from the coating, and the claimed method achieves this goal without producing a temperature that significantly degrades the active agent disposed in the coating or adversely affects the polymer in the coating**, which is an important technological advancement over the prior art.

Contrary to the Examiner's statement that the claimed range has no criticality, the Applicant has taught that the recited claimed range is in fact critical for the feasible use of the device. Additionally, the ability of the beam to modify (increase) the release rate of the bioactive agent certainly relates positively to the current density of the beam of charged particles. The extent of modification of release rate of the bioactive agent is similarly positively related to the current density of the beam of charged particles.

There is absolutely no teaching in Ding about "current density," and more significantly about preservation of the drug or polymeric matrix from degradation.

Ding not only fails to teach the claimed "current density," but to iterated, Ding fails to teach "directing" a beam as claimed. Applicants respectfully disagree with the Examiner's position that placement of a substrate in a plasma chamber at varying power ranges and flow rates is correlated to "directing a beam of charged particles" as claimed. **Ding describes a plasma treatment process in which a coated stent is placed in a reactor chamber and then an argon plasma is subsequently admitted into the chamber**. It is clear to an ordinary person skilled in the art that the argon plasma in **Ding would not be in the form of a beam, but rather a diffused flowing low pressure argon plasma environment**. For example, Ding describes the argon plasma as having a power range from 200 to 400 watts and a flow rate of 150-650 standard ml per minute, which is equivalent to about 100-450 mTorr, a very low pressure. Again, Applicant respectfully fails to see how Ding led the Examiner to conclude that it described a beam of charged particles rather than an argon plasma environment. Applicant preserves this issue for appeal.

In sum, Applicant believes that claim 27 is patentably allowable over Ding. Claims 28-33 and 35-37 depend from claim 27 and are patentably allowable over Ding for at least the same reasons.

Further, with respect to claim 31, the Examiner has noted that Ding includes "antithrombotics, anticoagulants, antiplatelet agents, thrombolytics, antiproliferatives, antinflammatories, and agents that inhibit hyperplasia and in particular restenosis." This teaching, the Examiner concludes, "reasonably suggests and motivates the instantly

claimed drivatives of rapamycin (which are know antiproliferatives and prevent restenosis)."

It is well-established law that disclosure of a genus in the prior art is not necessarily a disclosure of every species that is a member of that genus. Atofina v. Great Lakes Chemical Corp., 441 F.3d 991 (Fed.Cir. 2006). On the other hand, a very small genus can be a disclosure of each species within the genus. Sanofi-Synthelabo v. Apotex, 470 F.3d 1368 (Fed. Cir. 2006). Ding's disclosure engenders an **astronomical number** of possible drugs. Clearly, Ding does not render the use of 40-O-(2-hydroxy)ethyl-rapamycin obvious and but for an unsupported conclusion the Examiner has not provided any reasonable basis as to why one skilled in the art would choose this single species from an astronomical number of possible species.

With respect to claim 32, Ding fails to teach "wherein the beam is directed to only a portion of the coating along the length of the medical device."

With respect to claim 35, the Examiner has failed to provide why one skilled in the art would be motivated to subject Ding's coating to subsequent processing steps **after** it has been sterilized. Claim 35 recites, "further comprising forming a barrier layer over the dry coating **subsequent** to directing the beam of charged particles, the barrier layer comprising a polymer free from an active agent." The Examiner is equating the "directing the beam of charged particles" to Ding's sterilization process. Accordingly, why would one skilled in the art sterilize the device and coating and then deposit more coating on what has been sterilized? Sterilization step is conducted after all processing steps are finished and not in middle of manufacturing the device.

With respect to claim 37, Ding fails to teach "masking a portion of the coating prior to directing the beam of charged particles to eliminate or reduce the exposure of charged particles to the portion of the coating covered by the mask."

Claims 34 and 42 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Ding as applied to claims 27-33 and 35-37 above, and further in view of WO 03/022323. As indicated above, claim 27 is patentably allowable over Ding. The cited secondary reference WO 03/022323 does not cure the deficiencies of Ding with respect to claim 27. Accordingly, claim 27 is patentably allowable over the combination of the references. Claims 34 and 42 depend from claim 27 and are allowable or at least the same reason.

Claim 38 has been rejected under 35 U.S.C. 103(a) as being obvious over Ding as applied to claims 27-33 and 35-37, and in further view of EP 0970711. As indicated above, claim 27 is patentably allowable over Ding. The cited secondary reference EP 0970711 does not cure the deficiencies of Ding with respect to claim 27. Accordingly, claim 27 is patentably allowable over the combination of the references. Claim 38 depends from claim 27 and is allowable or at least the same reason.

Claims 39-41 have been rejected under 35 USC 103(a) as being obvious over Ding and in further view of U.S. Patent No. 6,120,847 to Yang et al. ("Yang"). As indicated above, claim 27 is patentably allowable over Ding. Yang does not cure the deficiencies of Ding with respect to claim 27. Accordingly, claim 27 is patentably allowable over the combination of the references. Claims 39-41 depend from claim 27 and are allowable or at least the same reason.

Additionally, the Examiner has failed to provide how Yang teaches the etchants

of claim 40.

Further, with respect to claims 39-41, the Examiner has failed to provide why one skilled in the art would be motivated to subject Ding's coating to subsequent processing steps **after** it has been sterilized. Claims 39-41 teach exposing the coating to a fluid or solvent after the charged particle process. The Examiner is equating the "directing the beam of charged particles" to Ding's sterilization process. Accordingly, why would one skilled in the art sterilize the device and coating and then subject the sterilized device to a fluid treatment? Sterilization step is conducted after all processing steps are finished and not in middle of manufacturing the device.

With respect to new claim 49, supported by page 13 of the specification, Ding alone or in combination with any of the cited references fails to teach "directing a beam of charged particles comprises directing different charged particle types to the dry polymeric coating."

With respect to new claim 50, supported by page 13 of the specification, Ding alone or in combination with any of the cited references fails to teach "wherein each of the different particles types are directed to the dry polymeric coating simultaneously."

With respect to new claim 51, supported by page 13 of the specification, Ding alone or in combination with any of the cited references fails to teach "wherein the different particles types are directed to the coating sequentially."

With respect to new claim 52, supported by page 11 of the specification, Ding alone or in combination with any of the cited references fails to teach "wherein the energy of the charged particles is between about 20 eV and about 15 MeV."

With respect to new claims 53 and 54, supported by page 12 of the specification,

Ding alone or in combination with any of the cited references fails to teach "wherein the beam of charged particles is directed to the coating at an angle of 20° to 80° to the coating surface" and "wherein the beams is directed to the coating at an angle of 90° to the coating surface."

With respect to claim 55, Ding teaches gamma radiation, electron beam, or plasma treatment. Accordingly, Ding cannot be used to reject claim 55 since it provides a proviso that the directing the beam of charged particles is not gamma radiation, electron beam, or plasma treatment. This claim is supported by page 10 of the specification which provides advantages of charged particles over gamma radiation and e-beam. Additionally, page 12 distinguishes between one embodiment that uses ion beam and another embodiment that uses plasma. Applicant, thus, can negatively claim applications that he does not wish to be included in the claims.

With respect to new claim 56, supported by page 11 of the specification, Ding alone or in combination with any of the cited references fails to teach "wherein the charged particles are selected from the group consisting of helium, oxygen, fluorine, titanium, nitrogen, antimony, uranium, krypton, xenon, gold and neon." Ding teaches argon, which has not been included in the Markush group.

With respect to new claim 57, supported by page 15 of the specification, Ding alone or in combination with any of the cited references fails to teach "wherein the duration of exposure is sufficient for increasing the release rate of the active agent in a patient by 10% to 25% as compared to if the coating was not subjected to directing a beam of charged particles."

With respect to new claim 58, supported by page 15 of the specification, Ding

alone or in combination with any of the cited references fails to teach "wherein the ion fluence of the charged particles is between about $10^3/cm^2$ to about $10^{16}/cm^2$."

With respect to new claim 59, supported by original claims 25 and 26, Ding alone or in combination with any of the cited references fails to teach "further comprising exposing the coating to a gas while exposing the coating to the charged particles, wherein the gas is selected from the group consisting of hydrogen, SO_2 and oxygen."

With respect to new claim 61, supported by page 22 of the specification, Ding alone or in combination with any of the cited references fails to teach "the charged particles create tracks that only penetrate through the barrier layer and stop at an upper surface of the dry coating."

CONCLUSION

Withdrawal of the rejection and allowance of the claims are respectfully requested. If the Examiner has any suggestions or amendments to the claims to place the claims in condition for allowance, applicant would prefer a telephone call to the undersigned attorney for approval of an Examiner's amendment. If the Examiner has any questions or concerns, the Examiner is invited to telephone the undersigned attorney.

Date: February 1, 2008

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